COPY FOR IB

PCT/KR2005/000016

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing *(day/month/year)*	21 APRIL 2005 (21.04.2005)
Applicant's or agent's file reference PCTA9501-1	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/KR2005/000016	05 JANUARY 2005 (05.01.2005)	05 JANUARY 2004 (05.01.2004)

International Patent Classification (IPC) or both national classification and IPC
IPC7 G01N 30/88

Applicant
Bio-MED Photonics Co., Ltd. et al

1. This opinion contains indications relating to the following items:

- [x] Box No. I Basis of the opinion
- [ ] Box No. II Priority
- [ ] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [x] Box No. IV Lack of unity of invention
- [x] Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI Certain documents cited
- [ ] Box No. VII Certain defects in the international application
- [x] Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**
If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.
For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/KR
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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material
   - ☐ a sequence listing
   - ☐ table(s) related to the sequence listing

   b. format of material
   - ☐ in wirtten format
   - ☐ in computer readable form

   c. time of filing/furnishing
   - ☐ contained in the international application as filed.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additioanl copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:
   - ☐ paid additional fees
   - ☐ paid additional fees under protest
   - ☐ not paid additional fees

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
   - ☐ complied with
   - ☐ not complied with for the following reasons:

The common concept linking together the independent Claims 1, 5 & 9 is the following:

including (a) a fluorescently-labeled detector reacts with analyte in liquid sample forming the fluorescently-labeled detector/analyte complex; (b) an unlabeled captor immobilized on the chromatographic medium reacts with the said complex forming the fluorescently-labeled detector/analyte/unlabeled captor triple complex; (c) a fluorescently-labeled reference detector reacts with a reference material in the liquid sample forming a reference complex and the complex further reacts with an unlabeled reference captor forming a reference triple complex; and (d) the amount of analytes is quantified by a laser-induced epifluorescence detection device as the fluorescence intensity of the triple complex of the analyte is being compared with that of the reference complex

Group I : Claims 1-11 The said common concept is apparently neither novel nor inventive. See under Box V.
Group II : Claims 12, dependent on Claim 9, features the window wall having a slope of 20 degree.
Group III : Claims 14 & 15, dependent on Claim 9, feature a time reading window on top plate of the cartridge housing.

The requisite unity of invention (Rule 13.1 PCT) therefore no longer exists between said Groups as far as a single inventive concept within the meaning of Rule 13.2 does not exist between Groups I-III.

4. Consequently, this opinion has been established in respect of the following parts of the international application :
   - ☐ all parts.
   - ☐ the parts relating to claims Nos. _____

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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	2, 3, 6, 7, 10 & 12-15	YES
	Claims	1, 4, 5, 8, 9 & 11	NO
Inventive step (IS)	Claims	12, 14 & 15	YES
	Claims	1-11 & 13	NO
Industrial applicability (IA)	Claims	1-15	YES
	Claims	none	NO

2. Citations and explanations :

Reference is made to the following documents from the International Search Report (ISR):
D1: WO 03062824 A1
D2: US 6136549 A
D3: US 5705338 A

Object of the present invention is to provide a method (Claim 1) and a strip (Claim 5) for the detection of lateral flow assay and a scanner (Claim 9) integrated with a laser-induced epifluorescence detection device.

1. Novelty
(i) regarding Claims 1, 4, 5, 8, 9 & 11
The subject matter of the present invention comprises constituents as recited in Claim 1 featuring a sandwich immunochromatographic method, which includes (a) a fluorescently-labeled detector reacts with analyte in liquid sample forming the fluorescently-labeled detector/analyte complex; (b) an unlabeled captor immobilized on the chromatographic medium reacts with the said complex forming the fluorescently-labeled detector/analyte/unlabeled captor triple complex; (c) a fluorescently-labeled reference detector reacts with a reference material in the liquid sample forming a reference complex and the complex further reacts with an unlabeled reference captor forming a reference triple complex; and (d) the amount of analytes is quantified by a laser-induced epifluorescence detection device as the fluorescence intensity of the triple complex of the analyte is being compared with that of the reference complex. The subject matters of Claims 5 & 9 also feature the aforementioned constituents.

D1 is considered the most relevant state of the art of the present invention in providing a lateral flow quantitative immunochromatography assay method, a strip and a detection means. D1 describes all the constituents of the subject matters of Claims 1, 5 & 9 (see in claims 1,8,18 & 30 of D1). D1 thus appears a novelty-destroying prior art. Claims 4, 8 & 11, which are dependent on Claims 1,5 & 9 respectively, are also disclosed in claims 4, 11 & 21 of D1 and therefore lack novelty.

Consequently, Claims 1, 4, 5, 8, 9 & 11 fail to fulfill the requirements set out in Article 33(2) PCT.
- continued in Supplemental box

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

1. Contrary to the requirements of Article 6 PCT, lack of clarity of Claims 2, 6 & 13 makes it extremely difficult, if not impossible, to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection:
"Ag line" of Claims 2, 6 & 13 is apparently interpreted as silver line (chemical code of silver is Ag) in light of description under [example 16] but should be regarded as acronym of antigen, given the problem set out in the present invention, one of which is to reduce "Hook effect" in sandwich assays especially when the analyte is present in an extremely high concentration and thereby saturates the unlabeled specific binder.

2. Contrary to the requirements of Article 6 PCT, description under [example 16] lacks clarity owing to the aforementioned reason.

3. Contrary to the requirements of Article 6 PCT, Claims 4, 8 & 11 lacks clarity making it difficult, if not impossible, to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection:
This authority believes that for detection of proteins present in test samples, "the captor" in said Claims is supposed to be the antibody against protein such as AFP, CEA, etc. but not one selected from those proteins.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of :

Box V

(ii) regarding Claims 2, 3, 6, 7, 10 & 12-15
Claims 3, 7 & 10 limit the unlabeled reference captor of Claims 1,5 & 9 to anti-mouse IgG, whereas use of anti-rabbit IgG is only disclosed in D1.
The dependent Claims 2, 6 & 12-15 impart the additional limitations to the subject matters of Claims 1,5 & 9, which are neither indicated in D1 nor directly inferred from the prior art.

Accordingly, Claims 2, 3, 6, 7, 10 & 12-15 meet the requirements set forth in Article 33(2) PCT.

2. Inventive step
(i) regarding Claims 1, 3-5 & 7-11
If novelty should be disputed based on some minor difference of interpretation, it is pointed out that the subject matter of Claims 1, 4, 5, 8, 9 & 11 would in any case not involve an inventive step. Because only slight modifications in constituents of said claims appear either to come within the scope of the customary practice followed by skilled persons in the art or to be what is easily achievable from the combination of D1 & D2, especially as the advantages thus achieved can readily be foreseen.

D2 discloses a system and a method for a lateral flow assay, wherein a test strip is analyzed by a photometer comprising a light source such as laser diodes and a fluorescence photodetector. Although D2 is directed to a magnetic chromatography assay method, which is alternative to the conventional assay system, D2 describes all the features of the conventional sandwich assay system, which constitute the subject matter of Claims 1, 5 & 9 (see in column 1, line 47 ~ column 5, line 11; column 11, line 23 ~ column 12, line 38; column 13, lines 18 ~ 67; and Figures 3a & 3b).

Regarding Claims 3, 7 & 10, it is believed that use of anti-mouse IgG as either captor or detector falls within the customary practice in the art and is thus obvious to a skilled person in the art. Furthermore, it is easily derivable from the combination of D1 & D2.

Therefore, Claims 1, 3-5 & 7-11 fail to fulfill the requirements set out in Article 33(3) PCT for the lack of inventive step.

(ii) regarding Claims 2, 6 & 13
Claims 2, 6 & 13 add to subject matter of Claims 1, 5 & 9, respectively, an immobilized Ag (Which is unclear but interpreted as antigen or analyte in this report) line, with which Ag or a detector reacts, taking into account the Hook effect. That is also considered a problem to be solved of D3. D3 indicates that the second zone containing an analyte derivative traps unreacted labeled specific binder only, and it thus corresponds to the Ag line of the present claims (see column 3, line 55 ~ column 4, line 19 and claims 6 & 7 in D3). Therefore, it is obvious to a person skilled in the art to arrive at the claimed invention through combining what D1 & D3 teach without exercising an inventive step. The advantage thus achieved is also foreseen.

Accordingly, Claims 2, 6 & 13 do not meet the criteria set forth in Article 33(3) PCT.

- continued in Supplemental box

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of :

Box V & Supplemental box

(iii) regarding Claims 12, 14 & 15
Claim 12 is about the scanner featuring the window wall having a slope of 20 degree.

Claims 14 & 15 are about the scanner featuring a time reading window on top plate of the cartridge housing.
The technical features are neither indicated nor suggested in prior art documents. It is unlikely to arrive at the claimed inventions even by combination of teachings from prior art unless exercising an inventive step. Advantages thus achieved in the present claims such as decreasing noise and variations in accuracy are considered unforseen over prior art.

Therefore, Claims 12, 14 & 15 meet the criteria set forth in Article 33(3) PCT.

3. Industrial applicability

Object of Claims 1-15 is to provide a method and a strip for the detection of lateral flow assay and a scanner, which are considered industrial applicable. Consequently, Claims 1-15 meet the requirements of Article 33(4) PCT.